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AMENDMENTS

Prior to further examination, please amend claim 38 as follows:

38. (Amended) A test device for determining the presence of a ligand in a liquid sample, the device comprising:

- a test strip comprising a sorbent material which defines a flow path for transporting a liquid sample therealong from a sample contact region to a test site and a control site, and, disposed upstream of said test site and said control site, a conjugate comprising the ligand or a binding analog thereof and a colored particulate material,

said test site comprising an immobilized first binding protein which binds the ligand, if present in the liquid sample, and said conjugate, and

said control site comprising an immobilized binder which binds said conjugate,

C wherein said sample contact region, said test site, and said control site are in lateral flow fluid communication through said flow path, such that after a liquid sample suspected to contain the ligand is applied to said sample contact region,

said conjugate moves along said flow path and binds said immobilized binder of said control site to produce a color visible to the unaided eye indicative of a valid test result, and

the ligand, if present in the liquid sample, or said conjugate binds to said immobilized first binding protein of said test site, said conjugate when bound at said test site, being visible to the unaided eye.

REMARKS

At the outset, Applicant wishes to thank Examiner Do for the courtesy extended and for the helpful discussions with the undersigned during a telephonic interview on September 20, 2001. The substance of the September 20, 2001 telephonic interview is incorporated herein.

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Claim 38 has been amended. Basis for the amendment may be found, for example, in the application as originally filed. This amendment merely clarifies that which Applicant considers to be his invention and is not required for patentability of the claimed subject matter. Applicant believes that the amendment introduces no new matter. Claims 27-39 presently are pending and under consideration in this application.

Applicant respectfully requests that the Examiner provide the undersigned with a copy of the PTO-1449 form filed January 8, 2001 with each citation initialed by the Examiner.

According to sections 3-5 of the outstanding Office Action, it appears that the respective rejections have been withdrawn.

Request for Correction of Inventorship

Please remove Neal Miller as a named inventor pursuant to 37 C.F.R. 1.48(b). The undersigned believes that Mr. Miller's contribution to the subject matter previously claimed in this application was primarily in the concept and design of the housing or casing as an optional integral part of the assay device useful in promoting ease of use, particularly by untrained consumers. The application as originally filed contained claims that required a casing (see, for example, claim 14 as filed). However, as a result of the January 8, 2001 submission, because the casing is no longer claimed in combination with the other elements of the invention in this application, Applicant believes that Mr. Miller should not properly be regarded as a co-inventor of the claimed subject matter, and requests his removal as an inventor pursuant to 37 C.F.R. 1.48(b). Authorization to charge deposit account number 20-0531 the fee prescribed by 37 C.F.R. 1.17(i) (\$130.00) is provided herewith.

Rejection of Claims 27-39 Under 35 U.S.C. §102(b)

According to sections 6 and 7 of the outstanding Office Action, claims 27-39 presently stand rejected under 35 U.S.C. §102(b) as being anticipated by Brown III et al. (EP 217 403 A). In view of the following remarks, Applicant respectfully requests that this rejection be reconsidered and withdrawn.

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It is well settled that a rejection under 35 U.S.C. §102(b) requires that all of the elements in the claim in their recited relationship be disclosed within the four corners of a single enabling reference. Applicant submits that the claims in the instant application clearly and explicitly require a device involving a test strip which supports lateral flow of a conjugate including a colored particulate material. After reviewing the applied art, Applicant submits that the foregoing features are neither disclosed nor even remotely suggested in the sole applied reference.

At the outset, Applicant submits that device described in Brown III is fundamentally different from the type of device embodied by the pending claims. For example, the device described in Brown III (see, Figure 1) is based on a well-type format where a liquid sample of interest is permitted to pass through a matrix located, for example, at the base of the well. In contrast, the device of the invention is an assay strip in which the liquid sample of interest, once applied to a sample contact region, traverses the test strip by lateral flow through a test site and a control site both of which are located away from the sample contact region. Some of the differences between the Brown III device and the claimed devices are discussed in more detail below.

First, a test strip which supports lateral flow is not disclosed in Brown III and is distinct from Brown's device, which supports flow vertically through a matrix as opposed to laterally on or within the surface of a matrix, web, or strip. Applicant submits that any slight lateral flow which may occur in the Brown III flow-through device is immaterial (or perhaps detrimental) to the functioning of the device, and does not anticipate even this element of the device claimed herein, as no flow path is involved.

This required feature of all claims herein is significant in that it permits a competitive or sandwich immunoassay to be conducted "automatically." Specifically, as the claims require, a liquid sample such as urine or other fluid, or a sample pre-treated or diluted in buffer or the like, can be applied to a sample contact region on the lateral flow test strip. Once applied, the liquid sample traverses the strip thereby conducting the steps of the immunoassay. Thus, for example, in claim 27, directed to a device designed to exploit sandwich immunoassay technology, the

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sample liquid passing along the test strip contains conjugate comprising the colored particles and encounters the test site where, in the presence of analyte or ligand, binding occurs.

In contrast, Brown III is limited to a flow-through device where the user first applies a sample to a given spot on the device, next applies a conjugate onto the same spot, next washes, and then applies an enzyme substrate (see, for example, Example 3 in Brown III). While Brown III envisions other formats, all require multiple sequential manipulative steps. The device claimed herein requires only the application of a liquid sample, or, in an alternative embodiment, premixing the conjugate with the liquid sample before application. All other steps occur automatically. In view of the foregoing, Applicant disagrees with the characterization in the Office Action that the Brown III matrix (12) "equates to the sorbent material which defines a flow path" of the claimed invention.

Second, all pending claims require the transport along a test strip of a conjugate comprising a colored particulate material which produces at the test site "color visible to the unaided eye." The assay devices claimed here are limited to the use of such colored particulate materials, such as gold sols, other metal sols or particles, polymeric particles, and the like. As disclosed in the specification, the particulate label when agglomerated at the test site produces a color visible to the unaided eye. No substrate addition is necessary to develop color.

Applicants submit that there is no disclosure of such labels in Brown III. While Brown III does disclose the use of particles in his device, they are neither colored nor used as labels in a conjugate. Furthermore, the Brown III particles are immobilized. In Brown III, Applicant submits that the particles are used to immobilize the binder for the analyte at the test site (see the examples and column 3, lines 52 through 57 of Brown III). In contrast, the particles of the claimed invention are not immobilized. During operation of a device of the claimed invention, conjugate comprising the colored particulate material "moves along the flow path."

From the foregoing it should be appreciated that it is not inherent in Brown III that "the test site and control site must be in lateral flow of communication." No significant lateral flow if at all is required in the Brown III device. See, for example, column 30, line 50 through column 31, line 48 of Brown III which discusses a "cross" type format and which makes clear that no lateral

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flow is required between the test site and the control site. Nor is it correct that "Brown's disk-shaped test strip performs the same function [and] inherently reads on the test strip of the invention." Nor is it correct that "Brown teaches....particulate labels (particles coated with first protein) [and] inherently reads on colored particles as being used as labels for the assay."

In view of the foregoing, Applicant submits that the rejection under 35 U.S.C. §102(b) is improper and requests that this rejection be reconsidered and withdrawn.

Double Patenting Rejection

According to sections 8 and 9 of the outstanding Office Action, claims 27-39 presently stand rejected under the judicially created doctrine of obviousness-type double patenting in view of claims 1-12 of U.S. Patent No. 5,989,921. Without acquiescing to the merits of this rejection, Applicant believes that the submission of the attached terminal disclaimer and authorization to charge the associated fee to deposit account 20-0531 obviates this rejection. Accordingly, Applicant respectfully requests that this rejection be reconsidered and withdrawn.

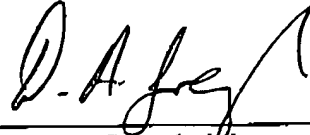
In order to complete the record, Applicant submits that related cases include: USSN 07/995,331, filed December 23, 1992 (now U.S. Patent No. 5,714,389), which is a continuation of USSN 07/702,450, filed May 16, 1991 (abandoned), which is a continuation of USSN 07/211,582, filed June 27, 1988 (abandoned); and USSN 08/465,675, filed June 6, 1995, which is a continuation of USSN 07/995,331, filed December 23, 1992 (now U.S. Patent No. 5,714,389), which is a continuation of USSN 07/702,450, filed May 16, 1991 (abandoned), which is a continuation of USSN 07/211,582, filed June 27, 1988 (abandoned). Applicants invite the Examiner to review these cases for double patenting issues.

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Conclusion

In view of the foregoing, Applicant respectfully submits that the case is in condition for immediate allowance.

Respectfully submitted,



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Marked-up Version of Amended Claim

38. (Amended) A test device for determining the presence of a ligand in a liquid sample, the device comprising:

a test strip comprising a sorbent material which defines a flow path for transporting a liquid sample therealong from a sample contact region to a test site and a control site, and, disposed upstream of said test site and said control site, a conjugate comprising the ligand or a binding analog thereof and a colored particulate material,

said test site comprising an immobilized first binding protein which binds the ligand, if present in the liquid sample, [or] and said conjugate, and

said control site comprising an immobilized binder which binds said conjugate,

wherein said sample contact region, said test site, and said control site are in lateral flow fluid communication through said flow path, such that after a liquid sample suspected to contain the ligand is applied to said sample contact region,

said conjugate moves along said flow path and binds said immobilized binder of said control site to produce a color visible to the unaided eye indicative of a valid test result, and

the ligand, if present in the liquid sample, or said conjugate binds to said immobilized first binding protein of said test site, said conjugate when bound at said test site, being visible to the unaided eye.